

## **Can Early Life Exposure to Permethrin lead to intergenerational effects?**

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### *Objectives*

Pesticides are largely used in agriculture against pests and consequently are present in fruits and vegetables. The wide presence of pesticide residues in breast milk underline the risk for the population, focalizing the long-term consequence of early life pyrethroid exposure.

The significant presence of pyrethroid metabolites in the urine of population over the world confirms that their presence in food is a global problem.

It has been demonstrated that there is a correlation between the environmental exposure to pesticides and the development of neurodegenerative diseases.

Neonatal exposure to Permethrin (PERM), a member of the family of synthetic pyrethroids, can induce neurodegeneration (i.e. Parkinson's -like disease) and it can cause some alterations in striatum of rats, involving both genetic and epigenetic pathways.

The aim of this study was to evaluate if the rat offspring (F1 generation) exposed to a low dose of PERM from postnatal day 6 to 21, presents alterations in Nurr1 gene expression as previously observed in early life permethrin treated male rats. Moreover, global DNA methylation was analyzed in untreated early life exposed mothers and offspring (F1 generation).

### *Methods*

Through Nurr1 gene expression analysis and global DNA methylation assessment in both PERM-treated parents and their untreated offspring, we investigated on the prospective intergenerational effect of this pesticide.

### *Results*

33% of progeny presents the same *Nurr1* alteration as rats exposed to permethrin in early life. A decrease in global genome-wide DNA methylation was measured in mothers exposed in early life to permethrin as well as in their offspring, whereas untreated rats have a hypermethylated genomic DNA.

### *Conclusions*

Intergenerational PERM-induced damage on progenies has been identified for the first time. On the light of these results, pesticide residues in the food could represent a risk factor for the health of children especially in early life when the brain is still in the developing phase. Further studies are needed to elucidate the molecular mechanisms associated with the damage.